What is claimed is:

Sub a1

1. A method for generating antibiotic resistant bacteria comprising the steps of :

blocking mismatch repair in a bacterium whereby said bacterium becomes hypermutable;

contacting said bacterium with at least one antibiotic;

selecting said a bacterium that is resistant to said antibiotic; and

culturing said bacterium;

thereby generating antibiotic resistant bacteria.

2. The method of claim 1 wherein said mismatch repair is blocked by introducing a dominant negative allele of a mismatch repair gene into said bacterium.

3. The method of claim 2 wherein said dominant negative allele of a mismatch repair gene is a *PMS2*-134 gene.

4. The method of claim 1 wherein said mismatch repair is blocked by introducing an antisense nucleic acid molecule into said bacterium wherein said antisense nucleic acid molecule specifically binds to a mismatch repair gene and inhibits mismatch repair in said bacterium.

5. The method of claim 1 wherein said mismatch repair is blocked by exposing said bacterium to a compound that inhibits mismatch repair.

6. The method of claim 5 wherein said compound is an anthracene derivative having the formula:

wherein R_1-R_{10} are independently hydrogen, hydroxyl, amino, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, O-alkyl, S-alkyl, N-alkyl, O-alkenyl, S-alkenyl, N-alkenyl,O-alkynyl, S-alkynyl, N-alkynyl, aryl, substituted aryl, aryloxy,

substituted aryloxy, heteroaryl, substituted heteroaryl, aralkyloxy, arylalkyl, alkylaryl, alkylaryloxy, arylsulfonyl, alkylsulfonyl, alkoxycarbonyl, aryloxycarbonyl, guanidino, carboxy, an alcohol, an amino acid, sulfonate, alkyl sulfonate, CN, NO_2, an aldehyde group, an ester, an ether, a crown ether, a ketone, an organosulfur compound, an organometallic group, a carboxylic acid, an organosilicon or a carbohydrate that optionally contains one or more alkylated hydroxyl groups;

wherein said heteroalkyl, heteroaryl, and substituted heteroaryl contain at least one heteroatom that is oxygen, sulfur, a metal atom, phosphorus, silicon or nitrogen;

wherein said substituents of said substituted alkyl, substituted alkenyl, substituted alkynyl, substituted aryl, and substituted heteroaryl are halogen, CN, NO_2, lower alkyl, aryl, heteroaryl, aralkyl, aralkyloxy, guanidino, alkoxycarbonyl, alkoxy, hydroxy, carboxy and amino; and

wherein said amino groups optionally substituted with an acyl group, or 1 to 3 aryl or lower alkyl groups.

7. The method of claim 6 wherein said compound is selected from the group consisting of 1,2-dimethylanthracene, 9,10-dimethyl anthracene, 7,8-dimethylanthracene, 9,10-diphenylanthracene, 9,10-dihydroxymethylanthracene, 9-hydroxymethyl-10-methylanthracene, dimethylanthracene-1,2-diol, 9-hydroxymethyl-10-methylanthracene-1,2-diol, 9-hydroxymethyl-10-methylanthracene-3,4-diol, 9,10-di-m-tolyanthracene.

8. The method of claim 6, further comprising exposing said bacterium to a chemical mutagen.

9. The method of claim 8 wherein said chemical mutagen is selected from the group consisting of methane sulfonate, dimethyl sulfonate, O-6-methyl benzadine, ethylnitrosourea, ethidium bromide, ethyl methanesulfonate, N-methyl-N'-nitro-N-nitrosoguanidine, methylnitrosourea, Tamoxifen, and 8-hydroxyguanine.

10. The method of claim 5 wherein said compound is selected from the group consisting of

an ATP analog, a nuclease inhibitor, and a DNA polymerase inhibitor.

11. The method of claim 10 wherein said ATP analog is selected from the group consisting of AMP-PNP and ATP[gamma]S.

12. The method of claim 10 wherein said nuclease inhibitor is selected from the group consisting of N-ethylmaleimide, heterodimeric adenine-chain-acridine compounds, exonulcease III inhibitors and heliquinomycin.

13. The method of claim 10 wherein said DNA polymerase inhibitor is selected from the group consisting of actinomycin D analogs, aphidicolin, 1-(2'-Deoxy-2'-fluoro-beta-L-arabinofuranosyl)-5-methyluracil, and 2',3'-dideoxyribonucleoside 5'-triphosphates.

14. The method of claim 1 wherein said antibiotic is a quinilone.

15. The method of claim 1 wherein said antibiotic is an aminoglycoside.

16. The method of claim 1 wherein said antibiotic is a magainin.

17. The method of claim 1 wherein said antibiotic is a defensin.

18. The method of claim 1 wherein said antibiotic is a tetracycline.

19. The method of claim 1 wherein said antibiotic is a beta-lactam.

20. The method of claim 1 wherein said antibiotic is a macrolide.

21. The method of claim 1 wherein said antibiotic is a lincosamide.

22. The method of claim 1 wherein said antibiotic is a sulfonamide.

23. The method of claim 1 wherein said antibiotic is a chloramphenicol.

24. The method of claim 1 wherein said antibiotic is a nitrofurantoin.

25. The method of claim 1 wherein said antibiotic is an isoniazid.

~~26. The method of claim 1 wherein the step of determining whether said bacterium is resistant to said antibiotic comprises analyzing said bacterium for multiantiboitic resistance.~~

27. The method of claim 1 further comprising making antibiotic resistant bacteria genetically stable.

28. The method of claim 5 further comprising making antibiotic resistant bacteria genetically stable.

29. The method of claim 28 wherein said antibiotic resistant bacteria are made genetically stable by removing the MMR inhibitory molecule.

30. A method for identifying a mutant gene conferring antibiotic resistance comprising comparing the genome of antibiotic resistant bacterium made by the method of claim 1 to the genome of a wild-type strain of said bacterium.

31. The method of claim 30 wherein the genome of said antibiotic resistant bacterium and the genome of said wild-type strain of said bacterium are compared by sequence analysis of the entire genomes.

32. The method of claim 30 wherein the genome of said antibiotic resistant bacterium and the genome of said wild-type strain of said bacterium are compared by microarray analysis.

33. The method of claim 30 wherein the genome of said antibiotic resistant bacterium and the genome of said wild-type strain of said bacterium are compared by:

introducing gene fragments from said antibiotic resistant bacterium into the wild-type bacterium, thereby producing mutant bacteria;

selecting a mutant bacterium with antibiotic resistance; and

sequencing said gene fragment from said mutant bacterium with antibiotic resistance, thereby identifying the antibiotic resistance gene.

34. The method of claim 30 wherein the genome of said antibiotic resistant bacterium and the genome of said wild-type bacterium are compared by:

introducing gene fragments from said wild-type strain of said bacterium into the antibiotic resistant strain of said bacterium;

selecting a mutant bacterium with antibiotic resistance; and

sequencing said gene fragment from said mutant bacterium, thereby identifying the antibiotic resistance gene.

35. A method of producing an antibiotic resistant bacterium comprising the steps of:

culturing bacteria with a natural defect in mismatch repair;

contacting said bacteria with at least one antibiotic;

selecting a bacterium among said bacteria resistant to said antibiotic; and

culturing said bacterium;

thereby generating antibiotic resistant bacteria.

36. A method of generating antibiotic resistant bacteria comprising the steps of:

overexpressing a mismatch repair gene in a bacterium whereby said bacterium becomes hypermutable;

contacting said bacterium with at least one antibiotic;

determining whether said bacterium is resistant to said antibiotic; and

culturing said bacterium;

thereby generating antibiotic resistant bacteria.

37. The method of claim 36 further comprising making said antibiotic resistant bacteria genetically stable.

38. An antibiotic resistant bacterium produced by the method of claim 1.

39. An antibiotic resistant bacterium produced by the method of claim 35.

40. An antibiotic resistant bacterium produced by the method of claim 36.

41. An antibiotic resistant bacterium produced by the method of claim 37.